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COGNITIVE IMPAIRMENT AFTER COVID-19 IN YOUNG PEOPLE

Cognitive impairment is one of the frequent neurological manifestations of post-COVID syndrome. **The aim** of this study was to assess cognitive impairment in young people after a mild novel coronavirus infection (COVID-19).

Materials and methods. The main group included 50 people with mild COVID-19 at the age of 19–35 years, incl. 17 (34%) men and 33 (66%) women. The control group included 50 people without a history of COVID-19, aged 18 to 33 years. All participants underwent neuropsychological testing: the Beck depression scale, the Spielberg questionnaire for identifying personal and situational anxiety, the subjective asthenia assessment scale (MFI-20), the 12-picture memory test, the 5-word memory test, the study of phonetic speech activity, and the Schulte test.

Research results. Study participants who had COVID-19 during the acute phase of the disease complained of general weakness (90%), headaches (86%), mental exhaustion (72%), muscle and joint pain (66%), decreased attention (64%), decreased sense of smell (62%), sleep disturbance (60%), apathy (54%), shortness of breath (34%) and chest pressure (26%). All complaints regressed after recovery, and their frequency did not differ from those of complaints in the control group. Neuropsychological examination revealed a somewhat higher level of depression (10.5 vs. 6.5 points on the Beck scale), some decrease in visual memory (11 vs. 11.5 pictures) and a higher incidence of general asthenia (74% vs. 44%) in patients COVID-19 ($p \leq 0.05$). There was no correlation between the severity of cognitive impairment and the duration of COVID-19.

Conclusions. COVID-19 is mildly accompanied by the development of mild cognitive impairment in young patients.

Keywords: cognitive impairment, COVID-19, depression, anxiety, asthenia.

Introduction. The outbreak of a new coronavirus infection began in December 2019 in Wuhan, Hubei Province (China), and on February 11, 2020, the World Health Organization recognized the outbreak of a new coronavirus disease as a pandemic and assigned the official name of the infection COVID-19 [2]. In Moscow, the first case of COVID-19 was registered on March 2, 2020, and on March 18, 2020, the first patient was detected in Yakutsk. [1]

Scientific observations have shown that in 70–76% of patients after infection, long-term consequences are possible with damage to one or more organs [11, 12]. In addition, with COVID-19, the central nervous system is affected more often than with other respiratory infections [3]. Chronic hypoxia, a pathological immune response, the direct damaging effect of the virus and the neurotropism of immune complexes, endothelial dysfunction of cerebral vessels, the state of the intestinal microbiota, and complications of drug therapy are considered as probable factors in the pathogenesis of neurological post-COVID syndrome [3, 5]. A wide range of neurological manifestations of coronavirus infection has been described in the form of asthenia, headaches, anosmia, insomnia, cognitive impairment, affective disorders, depression, and increased anxiety, which manifest themselves in 34% of people who have had COVID-19 [4, 8, 9]. Long-term monitoring of the health status of 1,733 patients in China by Huang C. et al. showed that weakness (63%), sleep disorders (26%), anxiety and depression (23%) are more common in post-COVID syndrome [14]. One of the most frequent complaints of patients after COVID-19 is a condition described by patients as "brain fog" and detected in 85.1% of cases [10]. At the same time, most of the studies were carried out mainly among people aged 40–65 years who had the disease in the acute stage in moderate and severe forms.

Currently, there are very few studies aimed at studying cognitive impairment after a new coronavirus infection among young people.

The aim of this study was to assess cognitive impairment in young people after a mild novel coronavirus infection (COVID-19).

Materials and research methods. A one-time study was conducted on the basis of the Department of Neurology and Psychiatry of the Medical Institute and the Laboratory of Neuropsychophysiological Research of the M.K. Ammosov North-Eastern Federal University. All participants signed a voluntary informed consent for inclusion in the study.

Inclusion criteria: 1) age of patients from 18 to 35 years; 2) a mild novel coronavirus infection (COVID-19); 3) absence of cognitive and affective complaints prior to COVID-19 disease.

Non-inclusion criteria: 1) the presence of neurological, mental and somatic diseases, which are accompanied by cognitive impairments and/or manifestations of which prevent the full implementation of the study protocol; 2) a new coronavirus infection (COVID-19) in moderate and severe severity; 3) the presence of cognitive complaints before COVID-19 disease; 4) the presence of migraine, tension headache before the disease.

The main group included 50 people with mild COVID-19 at the age of 19–35 years (median age 21.6 [19.8; 22.8] years, mean age 22.2 ± 4.4 year), incl. 17 (34%) men and 33 (66%) women. The control group included 50 people without a history of COVID-19, aged 18 to 33 years (median age 21.4 [19.2; 22.0] years, mean age 21.7 ± 3.2 years), including 15 (30%) men and 35 (70%) women. Both groups were statistically comparable in terms of sex and age ($p > 0.05$).

Assessment of cognitive functions was carried out using the following neuropsychological tests:

1) Beck depression scale. The presence of 10 or more points was regarded as the presence of depression;

2) Spielberg questionnaire to identify personal and situational anxiety;

3) Subjective scale for assessing asthenia (MFI-20). The analysis was carried out separately on subscales: general asthenia, reduced activity, decreased motivation, physical asthenia, psychological asthenia. If the total score on the subscale was 12 points or more, this indicated the presence of a pathology;

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4) Visual memory was assessed using a 12-picture memory test. Delayed recall (3 minutes after the interference task) and recognition (out of 48 presented images) were assessed.

5) Auditory memory was assessed using a 5-word memory test. Delayed playback and playback with categorical cues were evaluated.

6) Study of phonetic speech activity. The participant within one minute had to name words beginning with the letter "L" (except for proper names).

7) Methodology "Schulte Tables" for assessing attention.

Statistical processing of the results of the study was carried out using SPSS Statistics 22. Quantitative data are given as a median and the 25th and 75th quantiles (Me [Q25; Q75]). To compare two independent groups, the analysis was carried out using the Mann-Whitney U-test. When comparing qualitative data, Pearson's χ2 test and Fisher's exact test were used. Correlation analysis was carried out using Spearman's test. The critical level of statistical significance for the two groups was determined at $p \leq 0.05$.

Research results. The main group during the acute phase were treated on an outpatient basis and were included in the present study in the range from 12 to 800 days after recovery from COVID-19 (median - 167.5 [52.0; 466.5] days). Thirteen patients (26%) had recurrent disease. 41 (82%) patients of the main group and 45 (90%) patients of the control group were vaccinated against COVID-19 (p=0.249). All persons of the main group during the acute phase of the disease underwent computed tomography of the lungs, according to the results of which changes characteristic of COVID-19 were not detected.

Study participants who had COVID-19 during the acute phase of the disease complained of general weakness (90%), headaches (86%), mental exhaustion (72%), muscle and joint pain (66%), decreased attention (64%), decreased sense of smell (62%), sleep disturbance (60%), apathy (54%), shortness of breath (34%) and chest pressure (26%). All complaints regressed after recovery, and their frequency did not differ from those of complaints in the control group (table 1).

Neuropsychological examination revealed a slightly higher level of depression, some visual memory loss, and a higher incidence of generalized asthenia in COVID-19 survivors ($p \leq 0.05$). Representatives of the same group had higher assessment results for situational and personal anxiety, motivation, and asthe-

Table 1

Complaints in patients with COVID-19 and in the control group

Clinical presentation	Complaints in the acute phase of COVID-19	Complaints at the time of inclusion in the study	Control group	p-level
General weakness	45 (90)	14 (28)	9 (18)	$p_{1.2}<0.001$ $p_{2.3}=0.235$
Muscle/joint pain	33 (66)	8 (18)	7 (14)	$p_{1.2}<0.001$ $p_{2.3}=0.779$
Exhaustion during mental work	36 (72)	14 (28)	12 (24)	$p_{1.2}<0.001$ $p_{2.3}=0.648$
Decreased memory	29 (58)	22 (44)	15 (30)	$p_{1.2}=0.118$ $p_{2.3}=0.147$
Pressure in the chest	13 (26)	1 (2)	1 (2)	$p_{1.2}=0.002$ $p_{2.3}=1.0$
Dyspnea	17 (34)	5 (10)	6 (12)	$p_{1.2}=0.002$ $p_{2.3}=0.749$
Headache	43 (86)	18 (36)	23 (46)	$p_{1.2}<0.001$ $p_{2.3}=0.309$
Decreased sense of smell	31 (62)	5 (10)	1 (2)	$p_{1.2}<0.001$ $p_{2.3}=0.092$
Mood swings	20 (40)	13 (26)	11 (22)	$p_{1.2}=0.143$ $p_{2.3}=0.64$
Decreased attention	32 (64)	21 (42)	19 (38)	$p_{1.2}=0.013$ $p_{2.3}=0.683$
Decreased motivation	27 (54)	13 (26)	10 (20)	$p_{1.2}<0.001$ $p_{2.3}=0.476$
Anxiety	23 (46)	17 (34)	11 (22)	$p_{1.2}=0.146$ $p_{2.3}=0.181$
Sleep disturbance	30 (60)	15 (30)	16 (32)	$p_{1.2}<0.001$ $p_{2.3}=0.829$

Table 2

Neuropsychological examination of persons of the main and control groups

Clinical presentation	Main group, n = 50	Control group, n = 50	p-level
Beck Depression Scale, points	10.5 [6.0; 18.0]	6.5 [2.0; 14.3]	0.018*
Spielberg questionnaire, situational anxiety, scores	46.0 [35.8; 51.0]	39.0 [32.8; 48.3]	0.081
Spielberg questionnaire, personal anxiety, scores	51.5 [43.5; 57.0]	47.0 [41.0; 54.3]	0.096
Delayed visual memory, word count	11.0 [10.0; 12.0]	11.5 [11.0; 12.0]	0.046*
Delayed auditory memory, word count	4.5 [4.0; 5.0]	4.5 [4.0; 5.0]	0.937
Schulte Table technique, sec	25.0 [22.0; 30.5]	28.0 [23.7; 33.2]	0.08
Phonetic speech activity, number of words	12.5 [9.8; 15.0]	11.0 [8.8; 13.3]	0.07
General asthenia	37 (74%)	22 (44%)	0.002*
Reduced activity	30 (60%)	23 (46%)	0.161
Decreased motivation	22 (44%)	17 (34%)	0.305
Physical asthenia	24 (48%)	21 (42%)	0.546
Psychological asthenia	28 (56%)	25 (50%)	0.548

* Статистически значимый уровень (p≤0,05).

Table 3

Correlation analysis between the duration of COVID-19 and the results of neuropsychological test

	Depression on the Beck scale	Spielberg questionnaire, situational anxiety	Spielberg questionnaire, personal anxiety	Short-term visual memory	Attention "according to the Schulte table"	Short-term auditory memory
Correlation coefficient	0.274	0.182	0.033	0.051	-0.106	-0.274
p-level	0.054	0.207	0.818	0.725	0.465	0.234

nia, but a statistically significant level was not reached (Table 2).

To determine the relationship between the severity of cognitive impairment and the time after recovery, we conducted a correlation analysis. However, no relationship was found between the results of neuropsychological tests and the duration of COVID-19 (Table 3).

Discussion. According to the results of our study, in young people in the acute phase with a mild course of COVID-19, complaints from the nervous system predominate (for example, headaches, decreased attention, sense of smell, sleep disturbances). On the contrary, complaints of shortness of breath, pressure in the chest occur only in a third of patients.

According to a meta-analysis by J.P. Rogers, more than 18% of patients who survived the coronavirus of the Middle East respiratory syndrome had a decrease in concentration and memory impairment for a period of 6 to 39 months [13]. Pelen A.I. et al. studied the prevalence of cognitive and autonomic disorders of the nervous system among students of the Izhevsk State Medical Academy by the method of questioning. The study involved 139 people. The study was conducted by the MoCA neuropsychological test. According to the data obtained, it was found that cognitive disorders of the nervous system are more common in young people with a coronavirus infection than in those who have not been exposed to the disease [6].

Semenov V. A. et al. investigated cognitive impairment in young adults after suffering from COVID-19. They studied 172 apparently healthy people, aged 18–27 years on the MMSE scale. According to the results of the study, it was revealed that the pre-dementia state is quite common in young people, and moderate cognitive impairment is more common in people who have had a coronavirus infection [7].

The originality of our study is that we assessed the cognitive status of young people after mild COVID-19. We have shown that even after a mild course of COVID-19, disorders such as asthenia, mild depression, and a decrease in short-term visual memory are detected.

The main limitation of our work was the wide range of recency of COVID-19. Of course, a broad study is required with the division of patients according to the terms of recovery and the inclusion of neurophysiological methods of research, for example, cognitive evoked potentials. However, we have shown a general trend that, regardless of the duration of the disease, patients will have some or other impairments in the cognitive sphere.

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